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(FILE 'HOME' ENTERED AT 07:45:37 ON 28 DEC 1999)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, LIFESCI, HCAPLUS, NTIS, SCISEARCH' ENTERED AT 07:46:23 ON 28 DEC 1999

L1	874 S IDURONATE (2W)SULFATASE?
L2	3414 S L1 OR IDS
L3	138938 S GLYCOSYLAT?
L4	57343 S CHINESE HAMSTER OVARY?
L5	114122 S L4 OR CHO
L6	77284 S L5(W)CELL?
L7	24 S L2 AND L3
L8	24 S L7 AND L7
L9	0 S L7 AND L6
L10	3 S L5 AND L7
L11	3 DUP REM L10 (0 DUPLICATES REMOVED)
L12	11 DUP REM L7 (13 DUPLICATES REMOVED)
L13	11 S RECOMBINANT(W)L2
L14	2 S L13 AND L3
L15	2 DUP REM L14 (0 DUPLICATES REMOVED)
L16	5 DUP REM L13 (6 DUPLICATES REMOVED)
L17	9 S L13 AND FIBROBLAST?
L18	3 S L16 AND FIBROBLAST?
L19	3 DUP REM L18 (0 DUPLICATES REMOVED)
L20	11 S L7 AND FIBROBLAST?
L21	4 DUP REM L20 (7 DUPLICATES REMOVED)
L22	0 S COMPOSITION(P)L7
L23	0 S L7 AND COMPOSIT?
L24	0 S L16 AND COMPOSITION?
L25	88 S L2 AND COMPOSITION?
L26	1 S L25 AND RECOMBINANT
L27	0 S L25 AND L3

L11 ANSWER 1 OF 3 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD  
ACCESSION NUMBER: 1998-05849 BIOTECHDS  
TITLE: Treatment of **iduronate-2-sulfatase**  
deficiency;  
human recombinant enzyme preparation by expression in  
**CHO-K1**, or **Lec-1** cell, used for e.g. Hunter  
disease therapy or gene therapy  
AUTHOR: Wilson P J; Morris C P; Anson D S; Occhiodoro T;  
Bielicki J;  
Clements P R; Hopwood J J  
PATENT ASSIGNEE: Wilson P J; Morris C P; Anson D S; Occhiodoro T;  
Bielicki J;  
Clements P R; Hopwood J J  
LOCATION: North Adelaide, South Australia, Australia; Plympton,  
South  
Australia, Australia; Thebarton, South Australia,  
Australia;  
Prospect, South Australia, Australia.  
PATENT INFO: US 5728381 17 Mar 1998  
APPLICATION INFO: US 1995-484493 7 Jun 1995  
PRIORITY INFO: US 1995-484493 7 Jun 1995  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-206530 [18]

AB A new method for treating **iduronate-2-sulfatase** (  
**IDS**, EC-3.1.16.13) deficiency, e.g. Hunter disease, involves  
administering a human recombinant **IDS** that is more highly  
**glycosylated** than the naturally occurring enzyme. The  
recombinant **IDS** has better uptake properties and/or a longer  
half-life in vivo and is therefore more efficacious than naturally  
**glycosylated IDS**. Also disclosed are a human  
recombinant **IDS** with a defined 550 amino acid protein sequence  
and an isolated genomic DNA fragment carrying all or part of the  
**IDS** gene. Isolation of the genomic clone may enable gene therapy  
and genetic analysis of **IDS** deficiency diseases. Preferably,  
the recombinant **IDS** has a mol.wt. value of 70,000-90,000 by  
SDS-PAGE and is produced in **CHO-K1** or **Lec-1** cells. (53pp)

L11 ANSWER 2 OF 3 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD  
ACCESSION NUMBER: 1998-10390 BIOTECHDS  
TITLE: **Glycosylation** variants of **iduronate-2-**  
**sulfatase**;  
human recombinant enzyme preparation by  
vector-mediated  
gene transfer and expression in host cell, used for  
Hunter  
syndrome diagnosis or therapy  
AUTHOR: Wilson P J; Morris C P; Anson D S; Occhiodoro T;  
Bielicki J;  
Clements P R; Hopwood J J  
PATENT ASSIGNEE: Women's+Child.Hosp.North-Adelaide  
LOCATION: North Adelaide, South Australia, Australia.  
PATENT INFO: US 5798239 25 Aug 1998  
APPLICATION INFO: US 1995-484494 7 Jun 1995  
PRIORITY INFO: US 1995-484494 7 Jun 1995  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-480382 [41]  
AB A new method for producing a **glycosylated iduronate**  
**-2-sulfatase** (I, EC-3.1.6.13) with a mol.wt. value of  
65,000-95,000 involves culturing a host cell (e.g. **CHO-KI** or  
**CHO-Lec1** cells) containing a DNA sequence encoding the protein,  
where the host cell **glycosylates** the protein to a greater  
degree than an **iduronate-2-sulfatase** (II) naturally  
expressed in human liver cells, and where the mol.wt. value of (I) is

5,000-40,000 more than (II). A DNA sequence isolated from human endothelial cells disclosed. (I) deficiency in humans leads to the lysosomal accumulation of heparan sulfate and dermatan sulfate fragments and their excretion in urine. This storage causes Hunter syndrome (mucopolysaccharidosis type-II) in which patients may present variable phenotypes from severe mental retardation, skeletal deformities, and stiff joints, to a relatively mild course. (I) may be used to for diagnosis or therapy of (I)-associated diseases. (27pp)

L11 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:194978 HCAPLUS

DOCUMENT NUMBER: 128:261927

TITLE: **Glycosylation variants of iduronate 2-sulfatase**

INVENTOR(S): Wilson, Peter J.; Morris, Charles Phillip; Anson, Donald Stewart; Occhiodoro, Teresa; Bielicki, Julie;

PATENT ASSIGNEE(S): Clements, Peter Roy; Hopwood, John Joseph Australia

SOURCE: U.S., 53 pp. Division of U. S. Ser. No. 345,212. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5728381	A	19980317	US 1995-484493	19950607
✓US 5932211	A	19990803	US 1994-345212	19941128
US 5798239	A	19980825	US 1995-484494	19950607
PRIORITY APPLN. INFO.:			US 1991-790362	19911112
			US 1992-991973	19921217
			US 1994-345212	19941128

AB The present invention provides a highly **glycosylated iduronate-2-sulfatase** enzyme comprising an **iduronate-2-sulfatase** polypeptide with at least 5 kilodalton (kDa) more sugar than **iduronate-2-sulfatase** purified from a natural source, e.g. human liver. The present invention

also provides an enzymically active polypeptide fragment or variant of such a highly **glycosylated iduronate-2-sulfatase**. The present invention further provides an isolated nucleic acid encoding **iduronate-2-sulfatase**, as well as an expression vector, a host cell and a method for producing the present highly **glycosylated iduronate-2-sulfatase** enzyme. In one embodiment the present invention is directed to a method for producing a **glycosylated iduronate-2-sulfatase** enzyme which comprises culturing a host cell contg. a nucleic acid encoding an enzymically active **iduronate-2-sulfatase** polypeptide wherein the host cell **glycosylates** the polypeptide to a greater degree than a native **iduronate-2-sulfatase** polypeptide expressed by a natural human liver cell.

L12 ANSWER 8 OF 11 MEDLINE  
 ACCESSION NUMBER: 95351969 MEDLINE  
 DOCUMENT NUMBER: 95351969  
 TITLE: Processing of iduronate 2-sulphatase in human fibroblasts.  
 AUTHOR: Froissart R; Millat G; Mathieu M; Bozon D; Maire I  
 CORPORATE SOURCE: Centre d'Etudes des Maladies Metaboliques, Hopital Debrousse, Lyon, France..  
 SOURCE: BIOCHEMICAL JOURNAL, (1995 Jul 15) 309 ( Pt 2) 425-30.  
  
 Journal code: 9YO. ISSN: 0264-6021.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199511  
 AB Iduronate 2-sulphatase (**IDS**) is a lysosomal enzyme involved in degradation of dermatan sulphate and heparan sulphate. Antigenic material was obtained either by purification of placental **IDS** (A and B forms) or by expression of three different fusion peptides in Escherichia coli allowing the production of five specific antibodies. Pulse-chase-labelling experiments in over-expressing fibroblasts showed poor **IDS** processing but large amounts of precursors were secreted into the medium. The endocytosis of the 35S- or 33P-labelled precursors by deleted fibroblasts together with **glycosylation** studies and proteolysis inhibition by leupeptin allowed better elucidation of **IDS** maturation. The initial 73-78 kDa form is converted into a phosphorylated 90 kDa precursor after modification of its oligosaccharide chains in the Golgi apparatus. This precursor is processed by proteolytic cleavage through various intermediates to a major 55 kDa intermediate, with the release of an 18 kDa polypeptide. Further proteolytic cleavage by a thiol protease gives the 45 kDa mature form containing hybrid and complex-type oligosaccharide chains.

L12 ANSWER 1 OF 11 BIOSIS COPYRIGHT 1999 BIOSIS

ACCESSION NUMBER: 1999:443869 BIOSIS

DOCUMENT NUMBER: PREV199900443869

TITLE: **Glycosylation variants of iduronate 2-sulfatase.**

AUTHOR(S): Wilson, Peter J. (1); Morris, Charles Phillip; Anson, Donald Stewart; Occhiodoro, Teresa; Bielicki, Julie; Clements, Peter Roy; Hopwood, John Joseph

CORPORATE SOURCE: (1) Women's and Children's Hosp, North Adelaide Australia

PATENT INFORMATION: US 5932211 Aug. 03, 1999

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (Aug. 3, 1999) Vol. 1225, No. 1, pp. NO PAGINATION.

ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

L12 ANSWER 2 OF 11 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 1

ACCESSION NUMBER: 1999268795 EMBASE

TITLE: [DSM-IV disorders, metabolic control and somatic complications in insulin-dependent diabetes mellitus of child and adolescent].  
TROUBLES DSM-IV, EQUILIBRE METABOLIQUE ET COMPLICATIONS SOMATIQUES DANS LE DIABETE INSULINO-DEPENDANT DE

L'ENFANT

ET DE L'ADOLESCENT.

AUTHOR: Maronian S.; Vila G.; Robert J.-J.; Mouren-Simeoni M.-Ch.

CORPORATE SOURCE: G. Vila, Svc. Psychiat. l'Enfant/l'Adolescent, CHU Necker-Enfants Malades, 149, rue de Sevres, F-75015 Paris,

France

SOURCE: Annales Medico-Psychologiques, (1999) 157/5 (320-331).

Refs: 40

ISSN: 0003-4487 CODEN: AMPYAT

COUNTRY: France

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology

032 Psychiatry

LANGUAGE: French

SUMMARY LANGUAGE: English; French

AB Objectives: To describe the principal DSM-IV Mental Disorders, observed in

a work of a paediatric liaison, in a population of insulin-dependent diabetic (IDDM) children and adolescents, and their association, according

to the main diagnostic categories, with metabolic control and somatic complications; to study the relationship of familial environment socioeconomic status, age, sex of the patients and IDDM duration on metabolic control and somatic complications. Methods: We

retrospectively

included IDDM children and adolescents who have been systematically addressed in paedopsychiatry for three years for evaluation. They were 175

subjects, 96 girls and 79 boys, with a mean age of 13.5  $\pm$  4.5 years and

a mean IDDM duration of 4.9  $\pm$  3.9 years. They were assessed by clinical

interviews according with DSM-IV criteria. Metabolic control was measured

by **glycosylated** haemoglobin (HBAIC which is a reflect of the glycaemias of the last three months), at the first consultation in

paedopsychiatry and one year later. Somatic complications are systematically screened each year for all the IDDM patients (at least clinical examination, FO, retinal angiography, electroneurography and micro-albuminuria). Results: 102 patients (58.2%) had at least one

DSM-IV

disorder. The main disorders were anxiety disorders (33 subjects) and eating disorders (31 subjects); 24 subjects (13%) had affective disorders

and 17 (9%) had disruptive behaviour disorders. Children and adolescents

with mental disorders had a poorer metabolic control than others patients,

at the first psychiatric consultation and one year later. Affective disorders, disruptive behaviour disorders and eating disorders were significantly associated with a poor metabolic control (measured by higher

mean HBAIC), with a trend for patients with affective disorders and disruptive behaviour disorders to improve their HBAIC one year later. Patients with and without anxiety disorders had not significantly different HBAIC level. Familial problems, socioeconomic status and gender

were not associated with HBAIC level; age and IDDM duration were correlated with HBAIC. Somatic complications (retinopathy and others) were

associated with depressive disorders and an older age of the patients. Conclusions: This study shows that young IDDM patients did have DSM-IV disorders which were significantly associated with a poor metabolic control. So mental disorders should be systematically screened in

children

and adolescents with ID and be treated to help to improve their metabolic control and their quality of life.

L12 ANSWER 3 OF 11 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD  
ACCESSION NUMBER: 1998-05849 BIOTECHDS

TITLE: Treatment of **iduronate-2-sulfatase** deficiency;

human recombinant enzyme preparation by expression in CHO-K1, or Lec-1 cell, used for e.g. Hunter disease therapy or gene therapy

AUTHOR: Wilson P J; Morris C P; Anson D S; Occhiodoro T; Bielicki J;

Clements P R; Hopwood J J

PATENT ASSIGNEE: Wilson P J; Morris C P; Anson D S; Occhiodoro T; Bielicki J;

Clements P R; Hopwood J J

LOCATION: North Adelaide, South Australia, Australia; Plympton, South

Australia, Australia; Thebarton, South Australia, Australia;

Prospect, South Australia, Australia.

PATENT INFO: US 5728381 17 Mar 1998

APPLICATION INFO: US 1995-484493 7 Jun 1995

PRIORITY INFO: US 1995-484493 7 Jun 1995

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1998-206530 [18]

AB A new method for treating **iduronate-2-sulfatase** (

**ID**, EC-3.1.16.13) deficiency, e.g. Hunter disease, involves administering a human recombinant **ID** that is more highly

**glycosylated** than the naturally occurring enzyme. The

recombinant **ID** has better uptake properties and/or a longer

half-life in vivo and is therefore more efficacious than naturally

**glycosylated ID**. Also disclosed are a human

recombinant **ID** with a defined 550 amino acid protein sequence

and an isolated genomic DNA fragment carrying all or part of the

**ID** gene. Isolation of the genomic clone may enable gene therapy

and genetic analysis of **ID** deficiency diseases. Preferably,

the recombinant **ID** has a mol.wt. value of 70,000-90,000 by

SDS-PAGE and is produced in CHO-K1 or Lec-1 cells. (53pp)

L12 ANSWER 4 OF 11 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998-7090 BIOTECHDS

TITLE: **Glycosylation variants of iduronate-2-sulfatase;**

human recombinant enzyme preparation by  
vector-mediated gene transfer and expression in host cell, used for  
Hunter syndrome diagnosis or therapy

AUTHOR: Wilson P J; Morris C P; Anson D S; Occhiodoro T;  
Bielicki J;

Clements P R; Hopwood J J  
PATENT ASSIGNEE: Women's+Child.Hosp.North-Adelaide  
LOCATION: North Adelaide, South Australia, Australia.  
PATENT INFO: US 5798239 25 Aug 1998  
APPLICATION INFO: US 1995-484494 7 Jun 1995  
PRIORITY INFO: US 1995-484494 7 Jun 1995  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-480382 [41]

AB A new method for producing a **glycosylated iduronate-2-sulfatase** (I, EC-3.1.6.13) with a mol.wt. value of 65,000-95,000 involves culturing a host cell (e.g. CHO-KI or CHO-Lec1 cells) containing a DNA sequence encoding the protein, where the host cell **glycosylates** the protein to a greater degree than an **iduronate-2-sulfatase** (II) naturally expressed in human liver cells, and where the mol.wt. value of (I) is 5,000-40,000 more than (II). A DNA sequence isolated from human endothelial cells is disclosed.  
(I) deficiency in humans leads to the lysosomal accumulation of heparan sulfate and dermatan sulfate fragments and their excretion in urine. This storage causes Hunter syndrome (mucopolysaccharidosis type-II) in which patients may present variable phenotypes from severe mental retardation, skeletal deformities, and stiff joints, to a relatively mild course. (I) may be used to for diagnosis or therapy of (I)-associated diseases. (27pp)

L12 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:194978 HCAPLUS

DOCUMENT NUMBER: 128:261927

TITLE: **Glycosylation variants of iduronate 2-sulfatase**

INVENTOR(S): Wilson, Peter J.; Morris, Charles Phillip; Anson, Donald Stewart; Occhiodoro, Teresa; Bielicki, Julie;

Clements, Peter Roy; Hopwood, John Joseph

PATENT ASSIGNEE(S): Australia

SOURCE: U.S., 53 pp. Division of U. S. Ser. No. 345,212.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5728381	A	19980317	US 1995-484493	19950607
US 5932211	A	19990803	US 1994-345212	19941128
US 5798239	A	19980825	US 1995-484494	19950607
PRIORITY APPLN. INFO.:			US 1991-790362	19911112
			US 1992-991973	19921217
			US 1994-345212	19941128

AB The present invention provides a highly **glycosylated iduronate-2-sulfatase** enzyme comprising an **iduronate-2-sulfatase** polypeptide with at least 5 kilodalton (kDa) more sugar than **iduronate-2-sulfatase** purified from a natural source, e.g. human liver. The present invention

also provides an enzymically active polypeptide fragment or variant of such a highly **glycosylated iduronate-2-sulfatase**. The present invention further provides an isolated nucleic acid encoding **iduronate-2-sulfatase**, as well as an expression vector, a host cell and a method for producing the present highly **glycosylated iduronate-2-sulfatase** enzyme. In one embodiment the present invention is directed to a method for producing a **glycosylated iduronate-2-sulfatase** enzyme which comprises culturing a host cell contg. a nucleic acid encoding an enzymically active **iduronate-2-sulfatase** polypeptide wherein the host cell **glycosylates** the polypeptide to a greater degree than a native **iduronate-2-sulfatase** polypeptide expressed by a natural human liver cell.

L12 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 1999 ACS  
 ACCESSION NUMBER: 1997:100285 HCAPLUS  
 DOCUMENT NUMBER: 126:207933  
 TITLE: **IDS** transfer from overexpressing cells to **IDS**-deficient cells  
 AUTHOR(S): Millat, G.; Froissart, R.; Maire, I.; Bozon, D.  
 CORPORATE SOURCE: Centre d'etudes des Maladies Metaboliques, Hopital Debrousse, Lyon, 69322, Fr.  
 SOURCE: Exp. Cell Res. (1997), 230(2), 362-367  
 CODEN: ECREAL; ISSN: 0014-4827  
 PUBLISHER: Academic  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB **Iduronate sulfatase (IDS)** is responsible for mucopolysaccharidosis type II, a rare recessive X-linked lysosomal storage disease. The aim of this work was to test the ability of overexpressing cells to transfer **IDS** to deficient cells. In the first part of our work, **IDS** processing steps were compared in fibroblasts, COS cells, and lymphoblastoid cell lines and shown to be identical: the two precursor forms (76 and 90 kDa) were processed by a series of intermediate forms to the 55- and 45-kDa mature polypeptides. Then **IDS** transfer to **IDS**-deficient cells was tested either by incubation with cell-free medium of overexpressing cells or by coculture. Endocytosis and coculture expts. between transfected L.beta. and deleted fibroblasts showed that **IDS** transfer occurred preferentially by cell-to-cell contact as **IDS** precursors are poorly secreted by transfected L.beta.. The 76- and 62-kDa **IDS** polypeptides transferred to deleted fibroblasts were correctly processed to the mature 55- and 45-kDa forms. L.beta. were not able to internalize the 90-kDa phosphorylated precursor forms excreted in large amts. in the medium of overexpressing fibroblasts. Enzyme transfer occurred only by cell-to-cell contact, but the precursor forms transferred in L.beta. after cell-to-cell contact were not processed. This absence of maturation was probably due to a mistargeting of **IDS** precursors in these cells.

L12 ANSWER 7 OF 11 MEDLINE DUPLICATE 2  
 ACCESSION NUMBER: 97479223 MEDLINE  
 DOCUMENT NUMBER: 97479223  
 TITLE: Characterization of iduronate sulphatase mutants affecting N-glycosylation sites and the cysteine-84 residue.  
 AUTHOR: Millat G; Froissart R; Maire I; Bozon D  
 CORPORATE SOURCE: Centre d'etudes des Maladies Metaboliques, Hopital Debrousse, Lyon, France.  
 SOURCE: BIOCHEMICAL JOURNAL, (1997 Aug 15) 326 ( Pt 1) 243-7.



Journal code: 9YO. ISSN: 0264-6021.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199801  
 ENTRY WEEK: 19980104  
 AB Iduronate sulphatase (**IDS**) is responsible for mucopolysaccharidosis type II, a rare recessive X-linked lysosomal storage disease. The aim of this work was to evaluate the functional importance of each N-**glycosylation** site, and of the cysteine-84 residue. **IDS** mutant cDNAs, lacking one of the eight potential N-**glycosylation** sites, were expressed in COS cells. Although each of the potential sites was used, none of the eight **glycosylation** sites appeared to be essential for lysosomal targeting. Another important sulphatase co- or post-translational modification for generating catalytic activity involves the conversion of a cysteine residue surrounded by a conserved sequence C-X-P-S-R into a 2-amino-3-oxopropionic acid residue [Schmidt, Selmer, Ingendoh and von Figura (1995) Cell 82, 271-278]. This conserved cysteine, located at amino acid position 84 in **IDS**, was replaced either by an alanine (C84A) or by a threonine (C84T) using site-directed mutagenesis. C84A and C84T mutant cDNAs were expressed either in COS cells or in human lymphoblastoid cells deleted for the **IDS** gene. C84A had a drastic effect both for **IDS** processing and for catalytic activity. The C84T mutation produced a small amount of mature forms but also abolished enzyme activity, confirming that the cysteine residue at position 84 is required for **IDS** activity.

L12 ANSWER 8 OF 11 MEDLINE DUPLICATE 3  
 ACCESSION NUMBER: 95351969 MEDLINE  
 DOCUMENT NUMBER: 95351969  
 TITLE: Processing of iduronate 2-sulphatase in human fibroblasts.  
 AUTHOR: Froissart R; Millat G; Mathieu M; Bozon D; Maire I  
 CORPORATE SOURCE: Centre d'Etudes des Maladies Metaboliques, Hopital Debrousse, Lyon, France..  
 SOURCE: BIOCHEMICAL JOURNAL, (1995 Jul 15) 309 ( Pt 2) 425-30.

Journal code: 9YO. ISSN: 0264-6021.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199511  
 AB Iduronate 2-sulphatase (**IDS**) is a lysosomal enzyme involved in degradation of dermatan sulphate and heparan sulphate. Antigenic material was obtained either by purification of placental **IDS** (A and B forms) or by expression of three different fusion peptides in Escherichia coli allowing the production of five specific antibodies. Pulse-chase-labelling experiments in over-expressing fibroblasts showed poor **IDS** processing but large amounts of precursors were secreted into the medium. The endocytosis of the 35S- or 33P-labelled precursors by deleted fibroblasts together with **glycosylation** studies and proteolysis inhibition by leupeptin allowed better elucidation of **IDS** maturation. The initial 73-78 kDa form is converted into a phosphorylated 90 kDa precursor after modification of its oligosaccharide chains in the Golgi apparatus. This precursor is processed

by proteolytic cleavage through various intermediates to a major 55 kDa intermediate, with the release of an 18 kDa polypeptide. Further proteolytic cleavage by a thiol protease gives the 45 kDa mature form containing hybrid and complex-type oligosaccharide chains.

L12 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 1999 ACS  
ACCESSION NUMBER: 1995:694170 HCAPLUS  
DOCUMENT NUMBER: 123:109674  
TITLE: FIV vaccine studies. I. Immune response to recombinant FIV env gene products and outcome after challenge infection  
AUTHOR(S): Lutz, H.; Hofmann-Lehmann, R.; Bauer-Pham, K.; Holzmagel, E.; Tozzini, F.; Bendinelli, M.; Reubel, G.; Aubert, A.; Davis, D.; et al.  
CORPORATE SOURCE: Department Internal Veterinary Medicine, University Zurich, Zurich, Switz.  
SOURCE: Vet. Immunol. Immunopathol. (1995), 46(1,2), 103-13  
CODEN: VIIMDS; ISSN: 0165-2427  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The authors vaccinated five groups of cats (n = 25) four times with five prepns. of recombinant feline immunodeficiency virus (FIV) env gene products; one group (n = 7) served as control. The vaccine formulations were as follows: (1) envelope glycoprotein of FIV Zurich 2 (FIV Z2) expressed in a Baculovirus system and isolated by gel electroelution (denatured form); (2) insect cells expressing FIV Z2 glycoprotein; (3) envelope glycoprotein of a Boston strain (FIV Bangston) expressed in insect cells and isolated by gel electroelution (denatured form); (4) **glycosylated** Bangston envelope protein made in insect cells and isolated in a native form; (5) non-**glycosylated** Bangston envelope protein made in Escherichia coli. All cats were challenged with 20 50% cat IDs (CID50) of FIV Z2 previously titrated in cats. All vaccinated cats developed high ELISA antibodies to the homologous antigen; crossreactivity to heterologous antigens was seen at a lower level. Virus neutralizing antibodies (tested with Petaluma virus) reached titers up to 32. After challenge, all cats seroconverted (as judged by anti gag antibodies in Western blot) and became infected (as judged by virus isolation and/or polymerase chain reaction) between 4 and 11 wk with the exception of one cat. It is concluded that it is relatively easy to induce high ELISA antibody titers using recombinant env gene products, ELISA antibody titers do not correlate with virus neutralization or with protection.

L12 ANSWER 10 OF 11 MEDLINE  
ACCESSION NUMBER: 92095973 MEDLINE  
DOCUMENT NUMBER: 92095973  
TITLE: Morquio disease: isolation, characterization and expression of full-length cDNA for human N-acetylgalactosamine-6-sulfate sulfatase.  
AUTHOR: Tomatsu S; Fukuda S; Masue M; Sukegawa K; Fukao T; Yamagishi A; Hori T; Iwata H; Ogawa T; Nakashima Y; et al  
CORPORATE SOURCE: Department of Pediatrics, Gifu University School of Medicine, Japan.  
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1991 Dec 16) 181 (2) 677-83.

DUPLICATE 4



Jour. code: 9Y8. ISSN: 0006-291X.  
PUB. COUNTRY: Uni. States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
OTHER SOURCE: GENBANK-S70932; GENBANK-S70919; GENBANK-S74367;  
GENBANK-S67100; GENBANK-M64055; GENBANK-M64056;  
GENBANK-M64057; GENBANK-M64058; GENBANK-M64059;  
GENBANK-M64060  
ENTRY MONTH: 199204  
AB We cloned and sequenced a full-length cDNA of human placental  
N-acetylgalactosamine-6-sulfate sulfatase, the enzyme deficient in  
Morquio  
disease. The 2339-nucleotide sequence contained 1566 nucleotides which  
encoded a polypeptide of 522 amino acid residues. The deduced amino  
acid  
sequence was composed of a 26-amino acid N-terminal signal peptide  
and a  
mature polypeptide of 496 amino acid residues including two potential  
asparagine-linked **glycosylation** sites. Expression of the cDNA in  
transfected deficient fibroblasts resulted in higher production of  
this  
sulfatase activity than in untransfected deficient fibroblasts. The  
cDNA  
clone was hybridized to only a 2.3-kilobase species of RNA in human  
fibroblasts. The amino acid sequence of  
N-acetylgalactosamine-6-sulfate  
sulfatase showed a high degree of homology with those of other  
sulfatases  
such as human arylsulfatases A, B or C, glucosamine-6-sulfatase,  
**iduronate-2-sulfatase** and sea urchin arylsulfatase.

L12 ANSWER 11 OF 11 MEDLINE  
ACCESSION NUMBER: 81163947 MEDLINE  
DOCUMENT NUMBER: 81163947  
TITLE: Long-term, ambulatory, subcutaneous insulin infusion  
versus  
multiple daily injections in brittle diabetic  
patients.  
AUTHOR: Barbosa J; Menth L; Eaton J; Sutherland D; Freier E F;  
Najarian J  
CONTRACT NUMBER: AM-20742 (NIADDK)  
2-P01-AM13083 (NIADDK)  
RR-400 (NCRR)  
SOURCE: DIABETES CARE, (1981 Mar-Apr) 4 (2) 269-74.  
Journal code: EAG. ISSN: 0149-5992.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198108  
AB We compared the blood glucose control of four intact and eight kidney  
recipient, metabolically unstable, ketosis-prone, insulin-dependent  
diabetic patients under two different regimens: (a) intensive  
conventional  
treatment with two to four insulin injections daily (48  
patient-months)  
and (B) subcutaneous, portable insulin delivery system (**IDS**) (54  
patient-months). Both regimens included frequent home blood glucose  
and  
24-h urine glucose determinations and daily telephone follow-up to  
maximize compliance with treatment. Analyzed as a group the fasting  
blood  
glucose for intact patients (A: 172 +/- 13 mg/dl; B: 141 +/- 12, P  
less  
than 0.02) and the nonfasting blood glucose for kidney recipient  
patients  
(A: 165 +/- 10; B: 138 +/- 5, P less than 0.01) were significantly  
lower  
during treatment with the **IDS** than with multiple injections. Six  
out of 12 patients (2/4 intact and 4/8 kidney recipient patients)  
showed

*not selected*

significant and consistent improvement of blood glucose concentrations.

Four showed marginal and inconsistent improvement. Two patients (one intact and one kidney recipient) improved on the **IDS** but maintained the improvement when changed back to conventional treatment.

The 24-h urine glucose, maximal glucose excursions, number of blood glucoses less than or equal to 40 mg/dl, and **glycosylated** hemoglobin decreased significantly in some patients on the pump. We conclude that subcutaneous, portable insulin delivery devices can significantly improve the metabolic control of some ambulatory, unstable

diabetic patients during long-term treatment beyond that obtained with intensive, multiple-injection, conventional treatment. Normalization of

the metabolic control, however, is not obtained. These infusion systems

still pose several problems during ambulatory use, which could have serious consequences in patients less compliant and/or followed less closely than ours.

=> d 1-5 ibib ab

L16 ANSWER 1 OF 5 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD  
ACCESSION NUMBER: 1998-05849 BIOTECHDS  
TITLE: Treatment of iduronate-2-sulfatase deficiency;  
human recombinant enzyme preparation by expression in  
CHO-K1, or Lec-1 cell, used for e.g. Hunter disease  
therapy or gene therapy  
AUTHOR: Wilson P J; Morris C P; Anson D S; Occhiodoro T;  
Bielicki J;  
Clements P R; Hopwood J J  
PATENT ASSIGNEE: Wilson P J; Morris C P; Anson D S; Occhiodoro T;  
Bielicki J;  
Clements P R; Hopwood J J  
LOCATION: North Adelaide, South Australia, Australia; Plympton,  
South  
Australia, Australia; Thebarton, South Australia,  
Australia;  
Prospect, South Australia, Australia.  
PATENT INFO: US 5728381 17 Mar 1998  
APPLICATION INFO: US 1995-484493 7 Jun 1995  
PRIORITY INFO: US 1995-484493 7 Jun 1995  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-206530 [18]  
AB A new method for treating iduronate-2-sulfatase (IDS, EC-3.1.16.13)  
deficiency, e.g. Hunter disease, involves administering a human  
**recombinant IDS** that is more highly glycosylated than  
the naturally occurring enzyme. The **recombinant IDS**  
has better uptake properties and/or a longer half-life in vivo and is  
therefore more efficacious than naturally glycosylated IDS. Also  
disclosed are a human **recombinant IDS** with a defined  
550 amino acid protein sequence and an isolated genomic DNA fragment  
carrying all or part of the IDS gene. Isolation of the genomic  
clone may  
enable gene therapy and genetic analysis of IDS deficiency diseases.  
Preferably, the **recombinant IDS** has a mol.wt. value  
of 70,000-90,000 by SDS-PAGE and is produced in CHO-K1 or Lec-1  
cells.  
(53pp)

L16 ANSWER 2 OF 5 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD  
ACCESSION NUMBER: 1998-10390 BIOTECHDS  
TITLE: Glycosylation variants of iduronate-2-sulfatase;  
human recombinant enzyme preparation by  
vector-mediated  
gene transfer and expression in host cell, used for  
Hunter  
syndrome diagnosis or therapy  
AUTHOR: Wilson P J; Morris C P; Anson D S; Occhiodoro T;  
Bielicki J;  
Clements P R; Hopwood J J  
PATENT ASSIGNEE: Women's+Child.Hosp.North-Adelaide  
LOCATION: North Adelaide, South Australia, Australia.  
PATENT INFO: US 5798239 25 Aug 1998  
APPLICATION INFO: US 1995-484494 7 Jun 1995  
PRIORITY INFO: US 1995-484494 7 Jun 1995  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-480382 [41]  
AB A new method for producing a glycosylated iduronate-2-sulfatase (I,  
EC-3.1.6.13) with a mol.wt. value of 65,000-95,000 involves  
culturing a

host cell (e.g. CHO-K1 or CHO-Lec1 cells) containing a DNA sequence encoding the protein, where the host cell glycosylates the protein to a greater degree than an iduronate-2-sulfatase (II) naturally expressed in human liver cells, and where the mol.wt. value of (I) is 5,000-40,000 more than (II). A DNA sequence isolated from human endothelial cells is disclosed. (I) deficiency in humans leads to the lysosomal accumulation of heparan sulfate and dermatan sulfate fragments and their excretion in urine. This storage causes Hunter syndrome (mucopolysaccharidosis type-II) in which patients may present variable phenotypes from severe mental retardation, skeletal deformities, and stiff joints, to a relatively mild course. (I) may be used to for diagnosis or therapy of (I)-associated diseases. (27pp)

L16 ANSWER 3 OF 5 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD  
ACCESSION NUMBER: 1994-13487 BIOTECHDS

TITLE: Pre-clinical studies of lymphocyte gene therapy for  
Hunter

syndrome;  
human peripheral blood lymphocyte transduction with  
LSXN-derived retro virus vector for

iduronate-sulfatase

gene expression (conference abstract)

AUTHOR: Pan D; Braun S E; Jonsson J J; Aronovich E L; McIvor R S;  
Whitley C B

CORPORATE SOURCE: Univ.Minnesota-Med.Sch.

LOCATION: Gene Therapy Program, University of Minnesota Medical  
School,

Minneapolis, MN 55455, USA.

SOURCE: J.Cell.Biochem.; (1994) Suppl.18A, 244

CODEN: JCEBD5

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Retro virus constructs were studied and included: L2SN and LNC2  
(derived

from LXSN) with the iduronate-sulfatase (IDS) gene under the control  
of

the long terminal repeat or cytomegalo virus promoter; L2 with no  
selectable marker; and LB2 utilizing the beta-actin promoter.

Following

3.5 days of T-lymphocyte stimulation (OKT3, interleukin-2),  
peripheral

blood lymphocytes were transduced on 4 consecutive days with PA317  
supernatant in the presence of protamine sulfate. After culture for

3-6

days without G418 selection, peripheral blood lymphocytes were  
assayed

for IDS activity, tested for 35SO4-GAG accumulation versus time and  
co-cultured for 2 days to assess 35SO4-GAG accumulation in

neighboring

fibroblasts from patients with Hunter syndrome. IDS activity was  
increased in transduced cells above peripheral blood lymphocyte LXSN  
controls or leukocyte levels of patients and comparable to white

blood

cell levels of normal individuals. The transduced cells failed to  
show

continued accumulation of 35SO4-GAG, showing that **recombinant**  
**IDS** corrected the metabolic defect. Mild, non-neuropathic Hunter  
syndrome is suitable for ex vivo lymphocyte gene therapy. (0 ref)

L16 ANSWER 4 OF 5 MEDLINE

DUPLICATE 1

ACCESSION NUMBER: 94089725 MEDLINE

DOCUMENT NUMBER: 94089725

TITLE: Metabolic correction and cross-correction of  
mucopolysaccharidosis type II (Hunter syndrome) by

human                                   retroviral-mediated gene transfer and expression of  
  iduronate-2-sulfatase.  
AUTHOR:                               Braun S E; Aronovich E L; Anderson R A; Crotty P L;  
McIvor                                 R S; Whitley C B  
CORPORATE SOURCE:                   Department of Genetics and Cell Biology, University of  
  Minnesota, Minneapolis 55455..  
CONTRACT NUMBER:                   RO1DK39891 (NIDDK)  
SOURCE:                               PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE  
  UNITED STATES OF AMERICA, (1993 Dec 15) 90 (24)  
11830-4.

PUB. COUNTRY:                       Journal code: PV3. ISSN: 0027-8424.  
  United States  
  Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE:                            English  
FILE SEGMENT:                       Priority Journals; Cancer Journals  
ENTRY MONTH:                        199403

AB    To explore the possibility of using gene transfer to provide  
          iduronate-2-sulfatase (IDS; EC 3.1.6.13) enzyme activity for  
treatment of  
          Hunter syndrome, an amphotropic retroviral vector, L2SN, containing  
the  
          human IDS coding sequence was constructed and studied for gene  
expression  
          in vitro. Lymphoblastoid cell lines (LCLs) from patients with Hunter  
          syndrome were transduced with L2SN and expressed high levels of IDS  
enzyme  
          activity, 10- to 70-fold higher than normal human peripheral blood  
          leukocytes or LCLs. Such L2SN-transduced LCLs failed to show  
accumulation  
          of 35SO4 into glycosaminoglycan (35SO4-GAG), indicating that  
          **recombinant IDS** enzyme participated in GAG metabolism.  
          Coculture of L2SN-transduced LCLs with fibroblasts from patients with  
          Hunter syndrome reduced the accumulation of 35SO4-GAG. These results  
          demonstrated retroviral-mediated IDS gene transfer into lymphoid  
cells and  
          the ability of such cells to provide recombinant enzyme for  
intercellular  
          metabolic cross-correction.

L16   ANSWER 5 OF 5   BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1993-02607   BIOTECHDS

TITLE:                               Recombinant human iduronate-2-sulfatase: correction of  
  mucopolysaccharidosis-type-II fibroblasts and  
  characterization of the purified enzyme;  
  gene cloning and expression in CHO-K1 cell culture for  
  potential use in enzyme replacement therapy  
AUTHOR:                               Bielicki J; Hopwood J J; Wilson P J; \*Anson D S  
LOCATION:                               Lysosomal Diseases Research Unit, Department of Chemical  
  Pathology, Adelaide Children's Hospital, 72 King William  
  Road, North Adelaide, South Australia 5006, Australia.  
SOURCE:                               Biochem.J.; (1993) 289, Pt.1, 241-46  
  CODEN: BIJOAK

DOCUMENT TYPE:                       Journal  
LANGUAGE:                            English

AB    In order to evaluate enzyme replacement therapy for  
mucopolysaccharidosis  
          type-II, a chimeric iduronate-2-sulfatase (I2S, EC-3.1.6.13) cDNA was  
          cloned and expressed in a CHO-K1 cell culture, using a vector  
(plasmid  
          pB12Sc17) which placed the cDNA under the transcriptional control of  
the  
          human polypeptide chain elongation factor-1-alpha gene promoter. A  
cell  
          line that accumulated recombinant I2S at more than 10 mg/ml in  
          conditioned medium was identified. Cells were grown to confluency in  
          serum-free culture medium in two-layer cell factories, and  
recombinant  
          I2S was purified to homogeneity by PBE94 and Blue-A-agarose  
          chromatography, and by FPLC, resulting in purification of mg  
quantities

of recombinant I2S. The enzyme had a pH optimum and kinetic parameters similar to those for the mature form of I2S purified from human liver. The recombinant I2S had a mol.wt. of 90,000, which was reduced to 60,000 by deglycosylation using endoglycosidase. (11 ref)